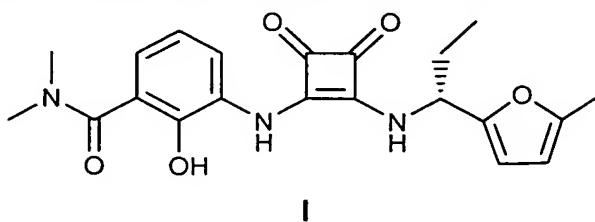


## CLAIMS

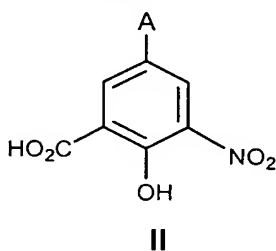
### What Is Claimed Is:

1. A process for preparing a compound of formula I:

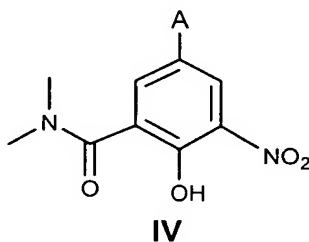


comprising:

- (a) converting the compound of formula II

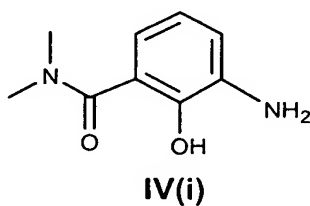


- 10 to a compound of formula IV:

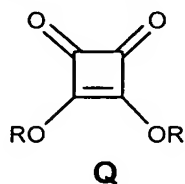


wherein A, in compounds of formulas II and IV, is selected from the group consisting of Br, Cl and I;

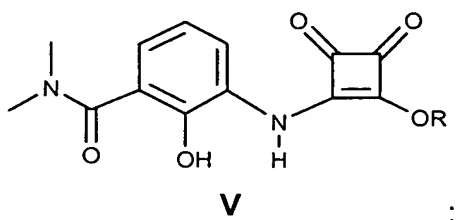
- 15 (b) hydrogenating the compound of formula IV with a suitable hydrogenation catalyst under hydrogen pressure, to form the intermediate compound of formula IV(i):



- (c) reacting the compound of formula **IV(i)** with a compound of formula **Q**:

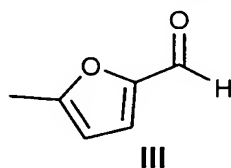


wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl, to yield a compound of formula **V**:

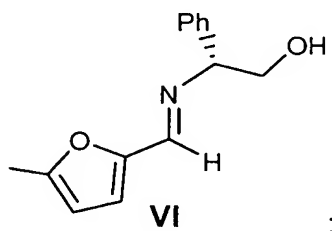


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- (d) converting the compound of formula **III**

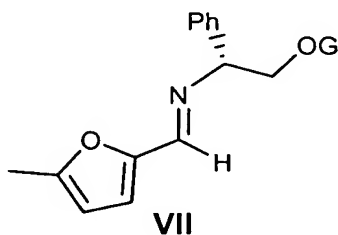


to a compound of formula **VI**:



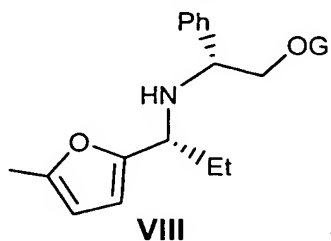
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- (e) adding a protecting group to the compound of formula **VI** to yield a compound of formula **VII**:



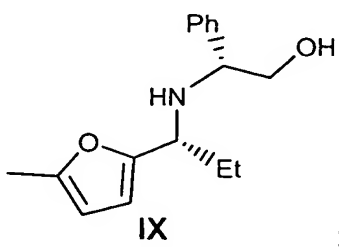
15 wherein G represents a protecting group;

(f) reacting the compound of formula **VII** with a suitable organometallic reagent, followed by work-up, to yield a compound of formula **VIII**:



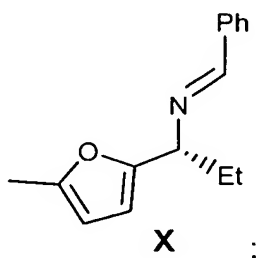
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(g) removing the protecting group (G) from the compound of formula **VIII** to yield a compound of formula **IX**:



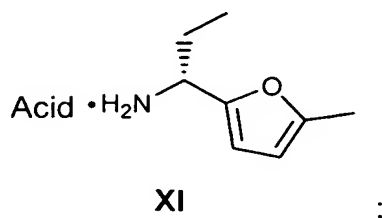
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(h) converting the compound of formula **IX** into an imine intermediate compound of formula **X**:



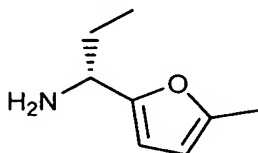
(i) converting the imine intermediate compound of formula **X** into the salt of formula **XI**:

15



(j) reacting the compound of formula **XI** with the compound of formula **V** to yield the compound of formula **I**; or

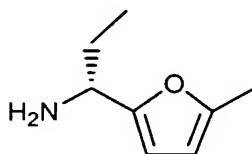
(k) converting the compound of formula **XI** to the free amine:



**XII**

and reacting the compound of formula **XII** with the compound of formula **V** to yield the compound of formula **I**.

2. The process of Claim 1 wherein said compound of formula **XI** in step (i) is converted to the compound of formula **XII**:



**XII**

by reacting said compound of formula **XI** in a suitable solvent with a suitable base, and then the compound of formula **XII** is reacted with the compound of formula **V** to produce the compound of formula **I**.

3. The process of Claim 1 wherein substituent A is Br.

4. The process of Claim 1 wherein G represents a protecting group selected from the group consisting of: silylating reagents and esters.

5. The process of Claim 1 wherein the acid in said compound of formula **XI** is selected from the group consisting of: sulfonic acids, tartaric acids, H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, HBr, and carboxylic acids, and mixtures thereof.

6. The process of Claim 1 wherein step (a) comprises reacting said compound of formula **II** with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine.

5 7. The process of Claim 1, wherein step (b) comprises making a mixture of said compound of formula **IV**, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under H<sub>2</sub> pressure.

10 8. The process of Claim 1 wherein step (c) comprises adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula **IV(i)** from step (b), adjusting the temperature to about 0°C to about 80°C to yield a compound of formula **V**.

15 9. The process of Claim 1 wherein step (d) comprises mixing a solution of R-2(-)-phenylglycinol with said compound of formula **III**, and heating the resulting solution at reflux with azeotropic removal of water to provide the imine compound of Formula **VI**.

20 10. The process of Claim 1 wherein step (e) comprises mixing an acid and a silylating reagent with the compound of formula **VI** from step (d), and heating the solution at reflux to provide a protected imine compound of formula **VII**.

25 11. The process of Claim 1 wherein the organometallic reagent, in step (f), is in a suitable solvent, and said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium.

30 12. The process of Claim 1 wherein step (g) comprises deprotecting the imine compound of formula **VIII** from step (f) with an acid, followed by treatment with a base to form said compound of formula **IX**.

13. The process of Claim 1 wherein step (h) comprises dissolving the compound of formula **IX** in a suitable solvent, adding R<sup>4</sup>NH<sub>2</sub>, and, following the

addition of said  $R^4NH_2$ , adding an additional agent selected from the group consisting of:  $NaIO_4$ ,  $Pb(OAc)_4$ ,  $H_5IO_6$ , and mixtures thereof, wherein  $R^4$  is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula **X**.

5

14. The process of Claim 1 wherein step (i) comprises (1) dissolving said intermediate compound of formula **X** from step (h) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula **XI**.

10

15. The process of Claim 1 wherein step (j) comprises combining the compound of formula **XI** from step (i), the compound of formula **V** from step (c), a suitable base and a suitable solvent, and heating the resulting reaction mixture to produce the compound of formula **I**.

15

16. The process of Claim 1 wherein in step (k) a catalytic amount of base is used in the reaction of the compound of formula **V** with the compound of formula **XII**.

17. The process of Claim 1 wherein:

(1) Substituent A is Br;

20

(2) G represents a protecting group selected from the group consisting of: silylating reagents and esters;

(3) Step (a) comprises reacting said compound of formula **II** with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine;

25

(4) Step (b) comprises making a mixture of said compound of formula **IV**, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under  $H_2$  pressure;

(5) Step (c) comprises adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula **IV(i)** from step (b), adjusting the temperature to about 0°C to about 80°C to yield a compound of formula **V**;

30

(6) Step (d) comprises mixing a solution of R-2-(-)-phenylglycinol with said compound of formula III, and heating the resulting solution at reflux with azeotropic removal of water to provide the imine compound of Formula VI;

(7) Step (e) comprises mixing an acid and a silylating reagent with the compound of formula VI from step (d), and heating the solution at reflux to provide a protected imine compound of formula VII;

(8) The organometallic reagent, in step (f), is in a suitable solvent, and said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium;

(9) Step (g) comprises deprotecting the imine compound of formula VIII from step (f) with an acid, followed by treatment with a base to form said compound of formula IX;

(10) Step (h) comprises dissolving the compound of formula IX in a suitable solvent, adding  $R^4NH_2$ , and, following the addition of said  $R^4NH_2$ , adding an additional agent selected from the group consisting of:  $NaIO_4$ ,  $Pb(OAc)_4$ ,  $H_5IO_6$ , and mixtures thereof, wherein  $R^4$  is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula X;

(11) Step (i) comprises (1) dissolving said intermediate compound of formula X from step (h) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula XI;

(12) Step (j) comprises combining the compound of formula XI from step (i), the compound of formula V from step (c), a suitable base and a suitable solvent, and heating the resulting reaction mixture to produce the compound of formula I; and

(13) Step (k) comprises using a catalytic amount of base in the reaction of the compound of formula V with the compound of formula XII.

18. The process of Claim 17 wherein:

(1) said solvent used with said acid chloride in step (a) is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform;

5 (2) said acid chloride in step (a) is selected from the group consisting of: thionyl chloride and oxalyl chloride;

(3) said dimethylamine in step (a) is a solution of dimethylamine wherein the solvent used in said dimethylamine solution is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene,  
10 ethylacetate, diethylether, and chloroform;

(4) said suitable base in step (b) is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof;

(5) said hydrogenation catalyst in step (b) is selected from the group  
15 consisting of: Pd/C, Pt/C, PdOH, and raney nickel;

(6) said 3,4-dialkoxy-3-cyclobutene-1,2-dione in step (c) is 3,4-diethoxy-3-cyclobutene-1,2-dione;

(7) said acid in step (e) is selected from the group consisting of: ammonium sulphate, ammonium nitrate, ammonium chloride, H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>,  
20 citric acid, mesylchloride, paratoluenesulfonic acid, paratoluenesulfonic acid pyridium salt, alkylsulfonic acid, and mixtures thereof;

(8) said silylating reagent in step (e) is selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein said TMS chloride is used in combination with triethylamine, and said TMSOTF is used in  
25 combination with triethylamine;

(9) said suitable solvent in step (f) is selected from the group consisting of: benzene, toluene, TBME, THF, DME, dimethoxyethane, and mixtures thereof;

(10) said acid in step (g) is selected from the group consisting of:  
30 H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, citric acid, ammonium chloride, and mixtures thereof;

(11) said base in step (g) is selected from the group consisting of: ammonium hydroxide, metal hydroxide, metal oxide, metal carbonate, metal



bicarbonate, and mixtures thereof, wherein said metal is selected from the group consisting of: lithium, sodium, potassium, rubidium, cesium, beryllium, magnesium, calcium, strontium, barium, aluminum, indium, thallium, titanium, zirconium, cobalt, copper, silver, zinc cadmium, mercury and cerium;

5                   (12) said acid in step (i) is selected from the group consisting of: sulfonic acids, tartaric acids,  $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{H}_3\text{PO}_4$ ,  $\text{HBr}$ , and carboxylic acids and mixtures thereof; and

                  (14) said base in step (k) is selected from the group consisting of: pyridine and  $\text{N}(\text{R}^3)_3$ , wherein each  $\text{R}^3$  is independently selected from the group  
10                   consisting of: alkyl, aryl and arylalkyl.

19.    The Process of Claim 18 wherein said acid in step (i) is a sulfonic acid selected from the group consisting of: paratoluene sulfonic acid and alkylsulfonic acid;

15           20.    The process of Claim 19 wherein said acid is paratoluene sulfonic acid.

21.    The process of Claim 18 wherein:

- 20           (1)    said acid chloride in step (a) is thionyl chloride;  
            (2)    said solvent used with said acid chloride in step (a) is acetonitrile;  
            (3)    said hydrogenation catalyst in step (b) is  $\text{Pd/C}$ ;  
            (4)    said acid in step (i) is paratoluene sulfonic acid; and  
            (5)    said base in step (k) is diisopropylethylamine;

22.    The process of Claim 18 wherein step (c) further comprises adding a  
25    base to the compound of formula **IV(i)**, wherein said base is selected from the group consisting of:  $\text{KOH}$ ,  $\text{NaOH}$ ,  $\text{Na}_2\text{CO}_3$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{NaHCO}_3$ ,  $\text{KHCO}_3$ , tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

23.    The process of Claim 20 wherein step (c) further comprises adding a  
30    base to the compound of formula **IV(i)**, wherein said base is selected from the group consisting of:  $\text{KOH}$ ,  $\text{NaOH}$ ,  $\text{Na}_2\text{CO}_3$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{NaHCO}_3$ ,  $\text{KHCO}_3$ , tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

24. The process of Claim 21 wherein step (c) further comprises adding a base to the compound of formula **IV(i)**, wherein said base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

5

25. The process of Claim 18 wherein:

- (1) said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula **II**;
- (2) said H<sub>2</sub> pressure in step (b) is from about 10 to about 500 psi;
- 10 (3) said 3,4-diethalkoxy-3-cyclobutene-1, 2-dione in step (c) is at least 1 molar equivalent with respect to the compound of formula **IV(i)**;
- (4) said R-2-(-)-phenylglycinol in step (d) is at least about 0.01 molar equivalent with respect to said compound of formula **III**;
- (5) said acid in step (e) is at least about 0.2 molar equivalent with respect to the compound of formula **VI**; and
- 15 (6) said organometallic reagent in step (f) is from about 0.1 to about 5 molar equivalents with respect to said compound of formula **VII**.

26. The process of Claim 21 wherein:

- 20 (1) said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula **II**;
- (2) said H<sub>2</sub> pressure in step (b) is from about 10 to about 500 psi;
- (3) said 3,4-diethalkoxy-3-cyclobutene-1, 2-dione in step (c) is at least 1 molar equivalent with respect to the compound of formula **IV(i)**;
- 25 (4) said R-2-(-)-phenylglycinol in step (d) is at least about 0.01 molar equivalent with respect to said compound of formula **III**;
- (5) said acid in step (e) is at least about 0.2 molar equivalent with respect to the compound of formula **VI**; and
- (6) said organometallic reagent in step (f) is from about 0.1 to about 30 5 molar equivalents with respect to said compound of formula **VII**.

27. The process of Claim 22 wherein:

- (1) said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula II;
- (2) said H<sub>2</sub> pressure in step (b) is from about 10 to about 500 psi;
- 5 (3) said 3,4-diethalkoxy-3-cyclobutene-1, 2-dione in step (c) is at least 1 molar equivalent with respect to the compound of formula IV(i);
- (4) said R-2-(-)-phenylglycinol in step (d) is at least about 0.01 molar equivalent with respect to said compound of formula III;
- (5) said acid in step (e) is at least about 0.2 molar equivalent with respect to the compound of formula VI; and
- 10 (6) said organometallic reagent in step (f) is from about 0.1 to about 5 molar equivalents with respect to said compound of formula VII.

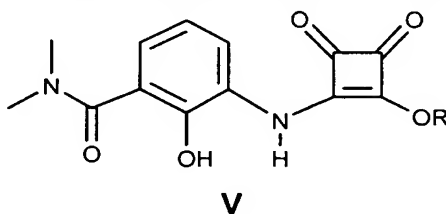
28. The process of Claim 21 wherein the compound of formula I is produced in step (k) by reacting the compound of formula XII with the compound of formula V.

29. The process of Claim 25 wherein the compound of formula I is produced in step (k) by reacting the compound of formula XII with the compound of formula V.

30. The process of Claim 26 wherein the compound of formula I is produced in step (k) by reacting the compound of formula XII with the compound of formula V.

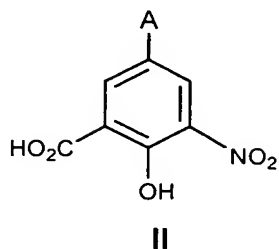
31. The process of Claim 27 wherein the compound of formula I is produced in step (k) by reacting the compound of formula XII with the compound of formula V.

32. A process for making a compound of formula V:

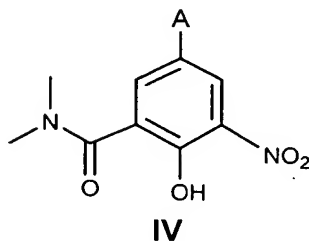


comprising:

- (a) converting the compound of formula II

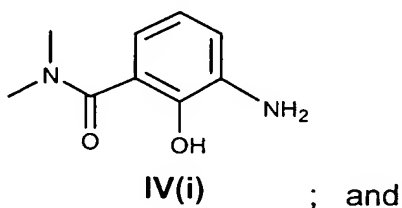


to a compound of formula IV:

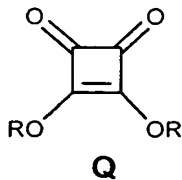


wherein A, in the compounds of formulas II and IV, is selected from the group consisting of Br, Cl and I;

- (b) hydrogenating the compound of formula IV with a suitable hydrogenation catalyst under hydrogen pressure, to form the intermediate compound of formula IV(i):



- (c) reacting the compound of formula IV(i) with a compound of formula Q:



wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl, to yield a compound of formula V.

33. The process of Claim 32 wherein substituent A is Br.

34. The process of Claim 32 wherein step (a) comprises reacting said compound of formula II with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine.

5 35. The process of Claim 32, wherein step (b) comprises making a mixture of said compound of formula IV, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under H<sub>2</sub> pressure.

10 36. The process of Claim 32 wherein step (c) comprises adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula IV(i) from step (b), adjusting the temperature to about 0°C to about 80°C to yield a compound of formula V.

15 37. The process of Claim 32 wherein step (c) further comprises adding a base to the compound of formula IV(i), wherein said base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

20 38. The process of Claim 32 wherein:

(1) said substituent A is Br;

25 (2) step (a) comprises reacting said compound of formula II with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine; said solvent used with said acid chloride is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform; said acid chloride is selected from the group consisting of: thionyl chloride and oxalyl chloride; and said dimethylamine is dimethylamine gas or a solution of dimethylamine wherein the solvent used in said dimethylamine solution is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform;

30 (3) step (b) comprises making a mixture of said compound of formula IV, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under

H<sub>2</sub> pressure; said suitable base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof; and said hydrogenation catalyst is selected from the group consisting of: Pd/C, Pt/C, PdOH, and raney nickel; and

5                   (4)     step (c) comprises adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula **IV(i)** from step (b), adjusting the temperature to about 0°C to about 80°C to yield a compound of formula **V**; said 3,4-dialkoxy-3-cyclobutene-1,2-dione is 3,4-diethoxy-3-cyclobutene-1,2-dione.

10           39.     The process of Claim 38 wherein:

- (1)     said acid chloride in step (a) is thionyl chloride;
- (2)     said solvent used with said acid chloride in step (a) is acetonitrile;

and

- (3)     said hydrogenation catalyst in step (b) is Pd/C

15           40.     The process of Claim 39 wherein step (c) further comprises adding a base to the compound of formula **IV(i)**, wherein said base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

20           41.     The process of Claim 40 wherein:

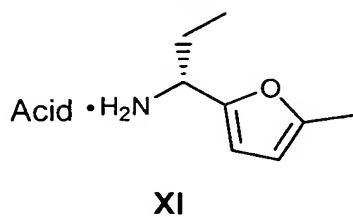
- (1)     said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula **II**;
- (2)     said H<sub>2</sub> pressure in step (b) is from about 10 to about 500 psi;

25     and

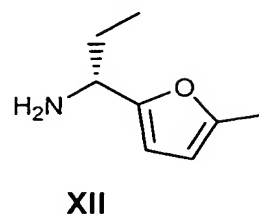
- (3)     said 3,4-diethalkoxy-3-cyclobutene-1, 2-dione in step (c) is at least 1 molar equivalent with respect to the compound of formula **IV(i)**.

30           42.     The process of Claim 41 wherein step (c) further comprises adding a base to the compound of formula **IV(i)**, wherein said base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof.

43. A process for making a compound of formula **XI** or **XII**:

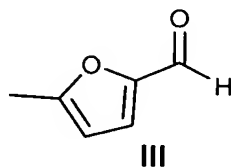


or

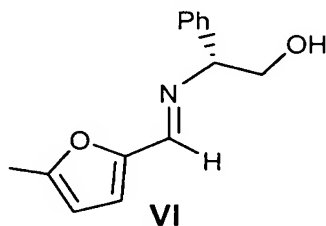


comprising:

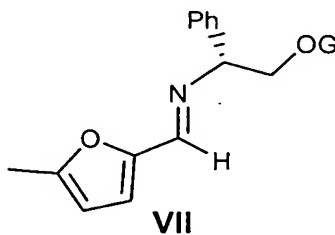
5 (a) converting the compound of formula **III**



to a compound of formula **VI**:

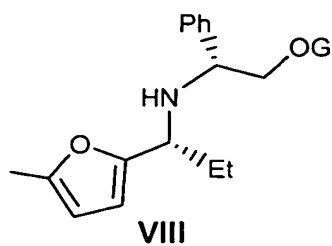


10 (b) mixing a protecting group with the compound of formula **VI** to yield a compound of formula **VII**:

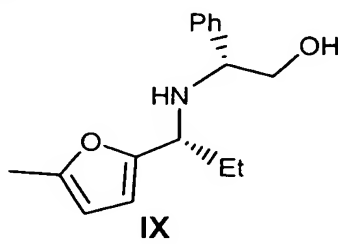


15 wherein G represents a protecting group;

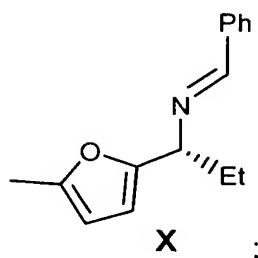
(c) reacting the compound of formula **VII** with a suitable organometallic reagent, followed by work-up, to yield a compound of formula **VIII**:



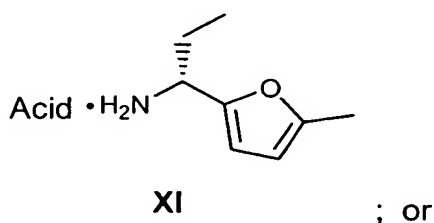
(d) removing the protecting group (G) from the compound of formula **VIII** to yield a compound of formula **IX**:



(e) converting the compound of formula **IX** into an imine intermediate compound of formula **X**:

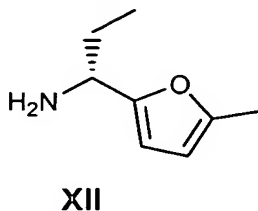


(f) converting the imine intermediate compound of formula **X** into the salt of formula **XI**:





- (g) converting the compound of formula **XI** to the free amine:



44. The process of Claim 43 wherein G represents a protecting group  
5 selected from the group consisting of: silylating reagents and esters.

45. The process of Claim 43 wherein the acid in said compound of formula  
**XI** is selected from the group consisting of: sulfonic acids, tartaric acids, H<sub>2</sub>SO<sub>4</sub>, HCl,  
H<sub>3</sub>PO<sub>4</sub>, HBr, and carboxylic acids, and mixtures thereof.

46. The process of Claim 43 wherein step (a) comprises mixing a solution of  
R-2-(-)-phenylglycinol with said compound of formula **III**, and heating the resulting  
solution at reflux with azeotropic removal of water to provide the imine compound of  
Formula **VI**.

47. The process of Claim 43 wherein step (b) comprises mixing an acid and  
a silylating reagent with the compound of formula **VI** from step (a), and heating the  
solution at reflux to provide a protected imine compound of formula **VII**.

48. The process of Claim 43 wherein the organometallic reagent, in step (c),  
is in a suitable solvent, and said organometallic reagent is selected from the group  
consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium  
bromide, ethylmagnesium chloride and ethyllithium.

49. The process of Claim 43 wherein step (d) comprises deprotecting the  
imine compound of formula **VIII** from step (c) with an acid, followed by treatment with  
a base to form said compound of formula **IX**.

50. The process of Claim 43 wherein step (e) comprises dissolving the compound of formula **IX** in a suitable solvent, adding  $R^4NH_2$ , and, following the addition of said  $R^4NH_2$ , adding an additional agent selected from the group consisting of:  $NaIO_4$ ,  $Pb(OAc)_4$ ,  $H_5IO_6$ , and mixtures thereof, wherein  $R^4$  is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula **X**.

51. The process of Claim 43 wherein step (f) comprises (1) dissolving said intermediate compound of formula **X** from step (e) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula **XI**.

52. The process of Claim 43 wherein:

(1) Step (a) comprises mixing a solution of R-2-(-)-phenylglycinol with said compound of formula **III**, and heating the resulting solution at reflux with azeotropic removal of water to provide the imine compound of Formula **VI**;

(2) Step (b) comprises mixing an acid and a silylating reagent with the compound of formula **VI** from step (a), and heating the solution at reflux to provide a protected imine compound of formula **VII**;

(3) The organometallic reagent, in step (c), is in a suitable solvent, and said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium;

(4) Step (d) comprises deprotecting the imine compound of formula **VIII** from step (c) with an acid, followed by treatment with a base to form said compound of formula **IX**;

(5) Step (e) comprises dissolving the compound of formula **IX** in a suitable solvent, adding  $R^4NH_2$ , and, following the addition of said  $R^4NH_2$ , adding an additional agent selected from the group consisting of:  $NaIO_4$ ,  $Pb(OAc)_4$ ,  $H_5IO_6$ , and mixtures thereof, wherein  $R^4$  is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula **X**; and

(6) Step (f) comprises (1) dissolving said intermediate compound of formula **X** from step (e) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula **XI**.

5 53. The process of claim 52 wherein:

(1) said acid in step (b) is selected from the group consisting of: ammonium sulphate, ammonium nitrate, ammonium chloride,  $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{H}_3\text{PO}_4$ , citric acid, mesylchloride, paratoluenesulfonic acid, paratoluenesulfonic acid pyridium salt, alkylsulfonic acid, and mixtures thereof;

10 (2) said silylating reagent in step (b) is selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein said TMS chloride is used in combination with triethylamine, and said TMSOTF is used in combination with triethylamine;

(3) said suitable solvent in step (c) is selected from the group  
15 consisting of: benzene, toluene, TBME, THF, DME, dimethoxyethane, and mixtures thereof;

(4) said acid in step (d) is selected from the group consisting of:  $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{H}_3\text{PO}_4$ , citric acid, ammonium chloride, and mixtures thereof;

(5) said base in step (d) is selected from the group consisting of:  
20 ammonium hydroxide, metal hydroxide, metal oxide, metal carbonate, metal bicarbonate, and mixtures thereof, wherein said metal is selected from the group consisting of: lithium, sodium, potassium, rubidium, cesium, beryllium, magnesium, calcium, strontium, barium, aluminum, indium, thallium, titanium, zirconium, cobalt, copper, silver, zinc cadmium, mercury and cerium; and

25 (6) said acid in step (f) is selected from the group consisting of: sulfonic acids, tartaric acids,  $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{H}_3\text{PO}_4$ ,  $\text{HBr}$ , and carboxylic acids, and mixtures thereof; and

54. The process of Claim 53 wherein:

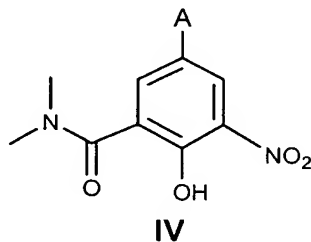
(1) said R-2-(-)-phenylglycinol in step (a) is at least about 0.01 molar equivalent with respect to said compound of formula III;

(2) said acid in step (b) is at least about 0.2 molar equivalent with respect to the compound of formula VI;

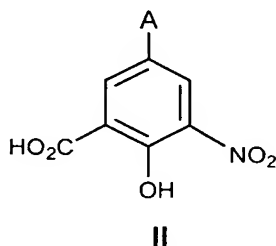
(3) said organometallic reagent in step (c) is from about 0.1 to about 5 molar equivalents with respect to said compound of formula VII; and

(4) said acid in step (d) is paratoluene sulfonic acid.

55. A process for making a compound of the formula:



comprising converting the compound of formula II



to a compound of formula IV, wherein A is selected from the group consisting of Br, Cl and I.

56. The process of Claim 55 wherein substituent A is Br.

57. The process of Claim 55 comprising reacting said compound of formula II with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine.

58. The process of Claim 55 wherein:

(1) said substituent A is Br;

(2) said compound of formula II is reacted with a suitable acid chloride in a suitable solvent at a suitable temperature, and then the resulting reaction mixture is reacted with dimethylamine; said solvent used with said acid chloride is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform; said acid chloride is selected from the group consisting of: thionyl chloride and oxalyl chloride; and said dimethylamine is dimethylamine gas or a solution of dimethylamine wherein the solvent used in said dimethylamine solution is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform.

59. The process of Claim 58 wherein:

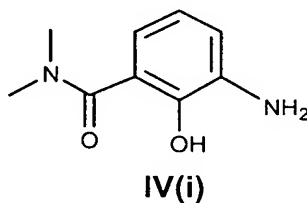
(1) said acid chloride in step (a) is thionyl chloride;

(2) said solvent used with said acid chloride in step (a) is acetonitrile;

and

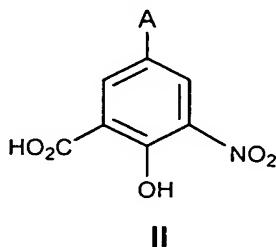
(3) said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula II.

60. A process for making a compound of formula IV(i):

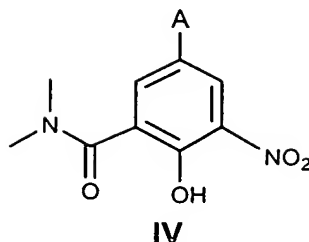


comprising:

(a) converting the compound of formula II



to a compound of formula **IV**:



wherein A, in compounds of formulas **II** and **IV**, is selected from the group consisting of Br, Cl and I; and

5

(b) hydrogenating the compound of formula **IV** with a suitable hydrogenation catalyst under hydrogen pressure, to form the compound of formula **IV(i)**.

10

61. The process of Claim 60 wherein substituent A is Br.

62. The process of Claim 60 wherein step (a) comprises reacting said compound of formula **II** with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine.

15

63. The process of Claim 60, wherein step (b) comprises making a mixture of said compound of formula **IV**, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under H<sub>2</sub> pressure.

20

64. The process of Claim 60 wherein:

(1) said substituent A is Br;

(2) step (a) comprises reacting said compound of formula **II** with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine; said solvent used with said acid chloride is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform; said acid chloride is selected from the group consisting of: thionyl chloride and oxalyl chloride; and said dimethylamine is dimethylamine gas or a solution of

25

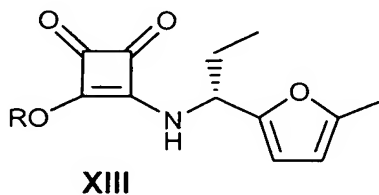
dimethylamine wherein the solvent used in said dimethylamine solution is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform; and

(3) step (b) comprises making a mixture of said compound of formula IV, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under H<sub>2</sub> pressure; said suitable base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof; and said hydrogenation catalyst is selected from the group consisting of: Pd/C, Pt/C, PdOH, and raney nickel.

65. The process of Claim 64 wherein:

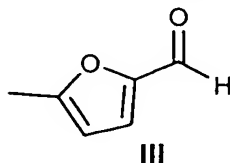
- (1) said acid chloride in step (a) is thionyl chloride;
- (2) said solvent used with said acid chloride in step (a) is acetonitrile;
- (3) said dimethylamine in step (a) is at a concentration of at least 1 molar equivalent with respect to said compound of formula II;
- (4) said hydrogenation catalyst in step (b) is Pd/C
- (5) said H<sub>2</sub> pressure in step (b) is from about 10 to about 500 psi.

66. A process for preparing a compound of the formula XIII:

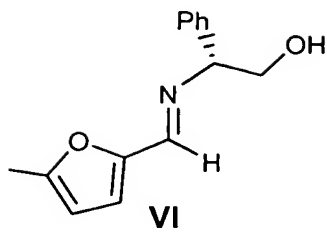


comprising:

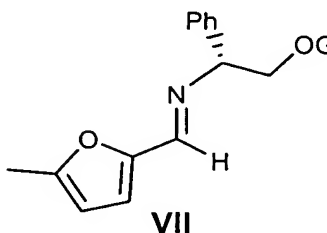
- (a) converting the compound of formula III



to a compound of formula **VI**:

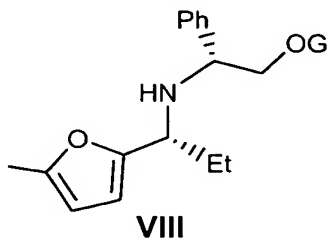


(b) adding a protecting group to the compound of formula **VI** to yield a compound of formula **VII**:



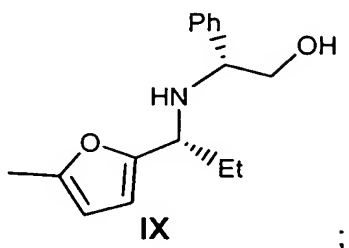
wherein G represents a protecting group;

(c) reacting the compound of formula **VII** with a suitable organometallic reagent, followed by work-up, to yield a compound of formula **VIII**:

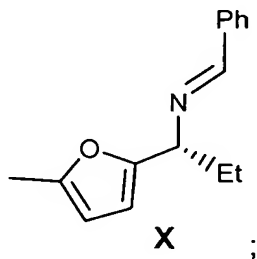




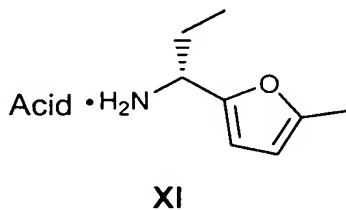
(d) removing the protecting group (G) from the compound of formula **VIII** to yield a compound of formula **IX**:



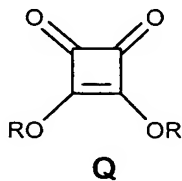
5 (e) converting the compound of formula **IX** into an imine intermediate compound of formula **X**:



10 (f) converting the imine intermediate compound of formula **X** into the salt of formula **XI**:

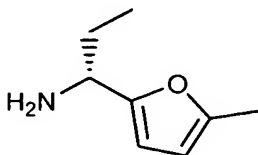


and reacting said compound of formula **XI** with a compound of formula **Q**:



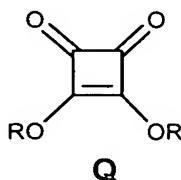
wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl to produce the compound of formula **XIII**; or

(g) converting the compound of formula **XI** to the free amine:



**XII**

by reacting the compound of formula **XI** in a suitable solvent with a suitable base, and reacting said compound of formula **XII** with **Q**:



wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl to produce the compound of formula **XIII**.

67. The process of Claim 66 wherein:

(1) Step (a) comprises mixing a solution of R-2-(-)-phenylglycinol with said compound of formula **III**, and heating the resulting solution at reflux with azeotropic removal of water to provide the imine compound of Formula **VI**;

(2) Step (b) comprises mixing an acid and a silylating reagent with the compound of formula **VI** from step (a), and heating the solution at reflux to provide a protected imine compound of formula **VII**;

(3) The organometallic reagent, in step (c), is in a suitable solvent, and said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium;

(4) Step (d) comprises deprotecting the imine compound of formula **VIII** from step (c) with an acid, followed by treatment with a base to form said compound of formula **IX**;

(5) Step (e) comprises dissolving the compound of formula **IX** in a suitable solvent, adding R<sup>4</sup>NH<sub>2</sub>, and, following the addition of said R<sup>4</sup>NH<sub>2</sub>, adding an additional agent selected from the group consisting of: NaIO<sub>4</sub>, Pb(OAc)<sub>4</sub>, H<sub>5</sub>IO<sub>6</sub>, and mixtures thereof, wherein R<sup>4</sup> is selected from the group consisting of alkyl, cycloalkyl,

heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula **X**;

(6) Step (f) comprises (1) dissolving said intermediate compound of formula **X** from step (e) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula **XI**, and then adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula **XI**, adjusting the temperature to about 0°C to about 80°C to yield a compound of formula **XIII**; and

(7) Step (g) comprises reacting the compound of formula **XII**, in a suitable solvent with a catalytic amount of a suitable base, with a 3,4-dialkoxy-3-cyclobutene-1,2-dione to yield a compound formula **XIII**.

68. The process of claim 67 wherein:

(1) said acid in step (b) is selected from the group consisting of: ammonium sulphate, ammonium nitrate, ammonium chloride, H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, citric acid, mesylchloride, paratoluenesulfonic acid, paratoluenesulfonic acid pyridium salt, alkylsulfonic acid, and mixtures thereof;

(2) said silylating reagent in step (b) is selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein said TMS chloride is used in combination with triethylamine, and said TMSOTF is used in combination with triethylamine;

(3) said suitable solvent in step (c) is selected from the group consisting of: benzene, toluene, TBME, THF, DME, dimethoxyethane, and mixtures thereof;

(4) said acid in step (d) is selected from the group consisting of: H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, citric acid, ammonium chloride, and mixtures thereof;

(5) said base in step (d) is selected from the group consisting of: ammonium hydroxide, metal hydroxide, metal oxide, metal carbonate, metal bicarbonate, and mixtures thereof, wherein said metal is selected from the group consisting of: lithium, sodium, potassium, rubidium, cesium, beryllium, magnesium, calcium, strontium, barium, aluminum, indium, thallium, titanium, zirconium, cobalt, copper, silver, zinc cadmium, mercury and cerium; and

(6) said acid in step (f) is selected from the group consisting of: sulfonic acids, tartaric acids,  $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{H}_3\text{PO}_4$ ,  $\text{HBr}$ , and carboxylic acids, and mixtures thereof; and

(7) said base in step (g) is selected from the group consisting of: pyridine and  $\text{N}(\text{R}^3)_3$ , wherein each  $\text{R}^3$  is independently selected from the group consisting of: alkyl, aryl and arylalkyl.

69. The process of Claim 68 wherein:

(1) said R-2-(-)-phenylglycinol in step (a) is at least about 0.01 molar equivalent with respect to said compound of formula III;

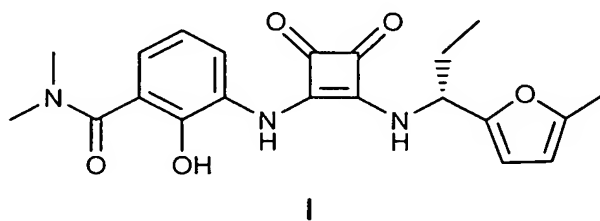
(2) said acid in step (b) is at least about 0.2 molar equivalent with respect to the compound of formula VI;

(3) said organometallic reagent in step (c) is from about 0.1 to about 5 molar equivalents with respect to said compound of formula VII;

(4) said acid in step (d) is paratoluene sulfonic acid; and

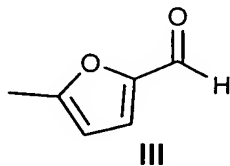
(5) said base in step (g) is diisopropylethylamine.

70. A process for producing a compound of the formula I:

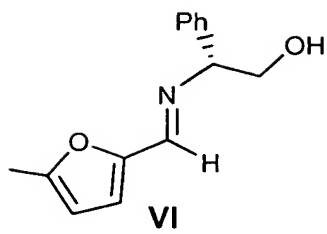


comprising:

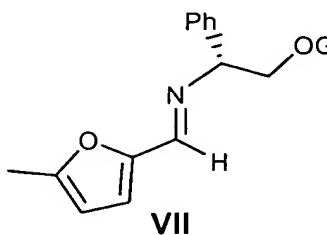
(a) converting the compound of formula III



to a compound of formula **VI**:

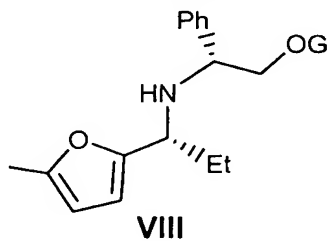


(b) adding a protecting group to the compound of formula **VI** to yield a compound of formula **VII**:

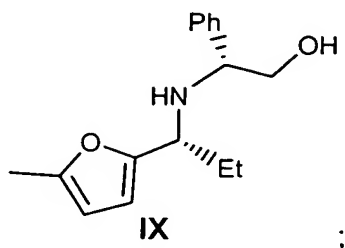


wherein G represents a protecting group;

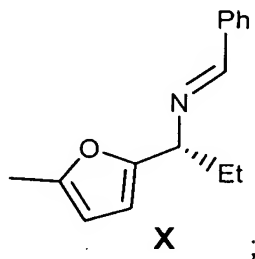
(c) reacting the compound of formula **VII** with a suitable organometallic reagent, followed by work-up, to yield a compound of formula **VIII**:



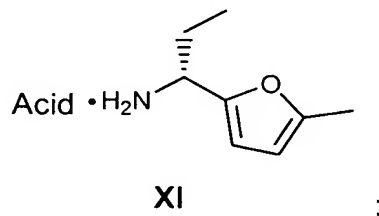
(d) removing the protecting group (G) from the compound of formula **VIII** to yield a compound of formula **IX**:



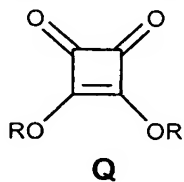
5 (e) converting the compound of formula **IX** into an imine intermediate compound of formula **X**:



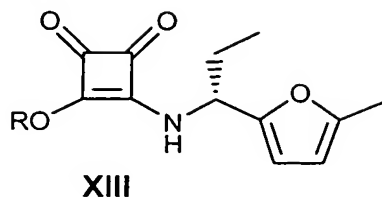
10 (f) converting the imine intermediate compound of formula **X** into the salt of formula **XI**:



(g) reacting the compound of formula **XI** with the compound of formula **Q**:

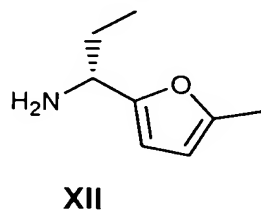


to yield a compound of formula **XIII**:

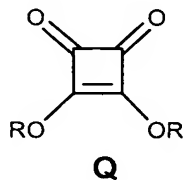


wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl in formulas **Q** and **XIII**; or

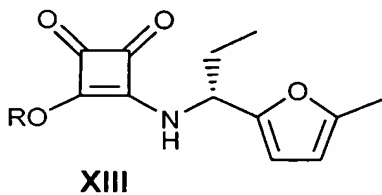
- 5 (h) converting the compound of formula **XI** to a compound of formula **XII**:



and reacting the compound of formula **XII** with a compound of formula **Q**:



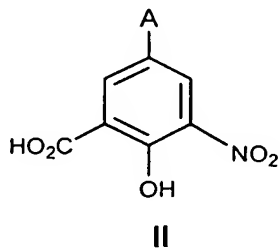
to yield a compound of formula **XIII**:



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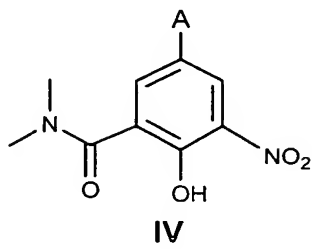
wherein R represents (C<sub>1</sub>-C<sub>10</sub>)alkyl in formulas **Q** and **XIII**;

- (i) converting the compound of formula **II**

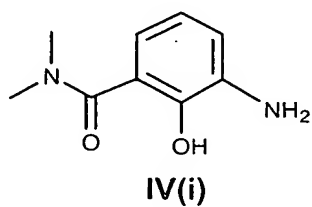


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wherein A is selected from the group consisting of Br, Cl and I, to a compound of formula **IV**:



- 5 (j) hydrogenating the compound of formula **IV** with a suitable hydrogenation catalyst under hydrogen pressure, to form the intermediate compound of formula **IV(i)**:



- 10 (k) reacting the compound of formula **IV(i)** with the compound of formula **XIII** to yield the compound of formula **I**.

71. The process of Claim 70 wherein:

- 15 (1) Step (a) comprises mixing a solution of R-2-(-)-phenylglycinol with said compound of formula **III**, and heating the resulting solution at reflux with azeotropic removal of water to provide the imine compound of Formula **VI**;
- (2) Step (b) comprises mixing an acid and a silylating reagent with the compound of formula **VI** from step (a), and heating the solution at reflux to provide a protected imine compound of formula **VII**;
- 20 (3) The organometallic reagent, in step (c), is in a suitable solvent, and said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium;



(4) Step (d) comprises deprotecting the imine compound of formula **VIII** from step (c) with an acid, followed by treatment with a base to form said compound of formula **IX**;

5 (5) Step (e) comprises dissolving the compound of formula **IX** in a suitable solvent, adding  $R^4NH_2$ , and, following the addition of said  $R^4NH_2$ , adding an additional agent selected from the group consisting of:  $NaIO_4$ ,  $Pb(OAc)_4$ ,  $H_5IO_6$ , and mixtures thereof, wherein  $R^4$  is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl, to provide the intermediate compound of formula **X**;

10 (6) Step (f) comprises (1) dissolving said intermediate compound of formula **X** from step (e) in a suitable solvent, and (2) adding a suitable acid to provide a compound of formula **XI**, and then adding 3,4-dialkoxy-3-cyclobutene-1,2-dione to said compound of formula **XI**, adjusting the temperature to about 0°C to about 80°C to yield a compound of formula **XIII**;

15 (7) Step (g) comprises reacting the compound of formula **XII**, in a suitable solvent with a catalytic amount of a suitable base, with a 3,4-dialkoxy-3-cyclobutene-1,2-dione to yield a compound formula **XIII**;

(8) Substituent A is Br in step (i);

20 (9) Step (i) comprises reacting said compound of formula **II** with a suitable acid chloride in a suitable solvent at a suitable temperature, and then reacting the resulting reaction mixture with dimethylamine;

(10) step (j) comprises making a mixture of said compound of formula **IV**, a hydrogenation catalyst, and a suitable base, and pressurizing the mixture under  $H_2$  pressure;

25 (11) Step (k) comprises reacting the compound of formula **XIII** with the compound of formula **IV(i)** at a suitable temperature to yield the compound of formula **I**.

72. The process of Claim 71 wherein:

(1) said acid in step (b) is selected from the group consisting of: ammonium sulphate, ammonium nitrate, ammonium chloride,  $H_2SO_4$ ,  $HCl$ ,  $H_3PO_4$ , citric acid, mesylchloride, paratoluenesulfonic acid, paratoluenesulfonic acid pyridium salt, alkylsulfonic acid, and mixtures thereof;

(2) said silylating reagent in step (b) is selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein said TMS chloride is used in combination with triethylamine, and said TMSOTF is used in combination with triethylamine;

(3) said organometallic reagent in step (c) is in a suitable solvent, said organometallic reagent is selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium, and said suitable solvent in step (c) is selected from the group consisting of: benzene, toluene, TBME, THF, DME, dimethoxyethane, and mixtures thereof;

(4) said acid in step (d) is selected from the group consisting of:  $H_2SO_4$ ,  $HCl$ ,  $H_3PO_4$ , citric acid, ammonium chloride, and mixtures thereof;

(5) said base in step (d) is selected from the group consisting of: ammonium hydroxide, metal hydroxide, metal oxide, metal carbonate, metal bicarbonate, and mixtures thereof, wherein said metal is selected from the group consisting of: lithium, sodium, potassium, rubidium, cesium, beryllium, magnesium, calcium, strontium, barium, aluminum, indium, thallium, titanium, zirconium, cobalt, copper, silver, zinc cadmium, mercury and cerium; and

(6) said acid in step (f) is selected from the group consisting of: sulfonic acids, tartaric acids,  $H_2SO_4$ ,  $HCl$ ,  $H_3PO_4$ ,  $HBr$ , and carboxylic acids, and mixtures thereof;

(7) said solvent used with said acid chloride in step (i) is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform;

(8) said acid chloride in step (i) is selected from the group consisting of: thionyl chloride and oxalyl chloride;

(9) said dimethylamine in step (i) is dimethylamine gas or a solution of dimethylamine wherein the solvent used in said dimethylamine solution is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform;

5 (10) a suitable base is used in step (j) and said base is selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof; and

(11) said hydrogenation catalyst in step (j) is selected from the group consisting of: Pd/C, Pt/C, PdOH, and raney nickel.

10 73. The process of Claim 72 wherein:

(1) said R-2-(-)-phenylglycinol in step (a) is at least about 0.01 molar equivalent with respect to said compound of formula III;

15 (2) said acid in step (b) is at least about 0.2 molar equivalent with respect to the compound of formula VI;

(3) said organometallic reagent in step (c) is from about 0.1 to about 5 molar equivalents with respect to said compound of formula VII;

(4) said acid in step (d) is paratoluene sulfonic acid;

(5) said acid chloride in step (i) is thionyl chloride;

20 (6) said solvent used with said acid chloride in step (i) is acetonitrile;

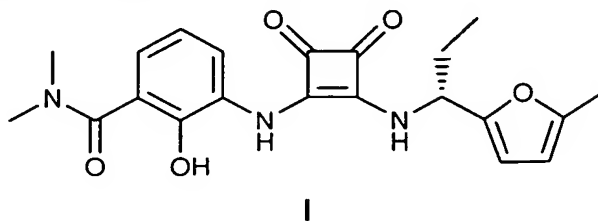
(7) said dimethylamine in step (i) is at a concentration of at least 1 molar equivalent with respect to said compound of formula II;

(8) said hydrogenation catalyst in step (j) is Pd/C; and

(9) said H<sub>2</sub> pressure in step (j) is from about 10 to about 500 psi.

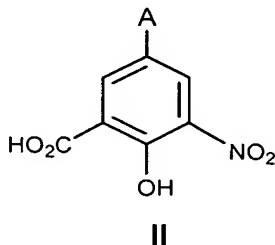
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74. A process for preparing a compound of formula I:



5 comprising:

(a) dissolving the compound of formula II:



in:

10 a solvent selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform, and

an acid chloride selected from the group consisting of: thionyl chloride and oxalyl chloride, wherein a catalytic amount of DMF is optionally used when oxalyl chloride is used;

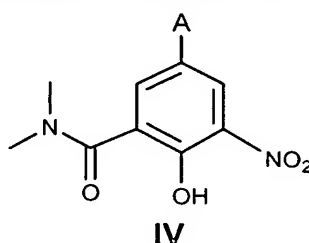
and adjusting the temperature of the resulting reaction mixture to a about -20°C to about 110°C;

cooling the reaction mixture, when the reaction is complete, to a temperature of about 5°C to about 10°C;

20 adding dimethylamine gas or a solution of dimethylamine, at a concentration of at least about 1 molar equivalent with respect to the compound of formula II, wherein the solvent used in said dimethylamine is selected from the group consisting of: acetonitrile, THF, t-butylmethylether, methylenechloride, toluene, ethylacetate, diethylether, and chloroform;

adjusting the temperature of the resulting reaction mixture to a temperature of about -20°C to about 50°C;

acidifying the resulting reaction mixture with an aqueous acid to a pH of about 0 to about 7, to produce a compound of formula **IV**:



wherein A is in the compounds of formulas **II** and **IV** is selected from the group consisting of Br, Cl and I;

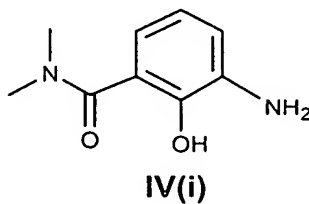
(b) hydrogenating the compound of formula **IV** by mixing said compound of formula **IV** with:

a base selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine and mixtures thereof, wherein said base is in a concentration of at least about 1 molar equivalent with respect to the compound of formula **IV**,

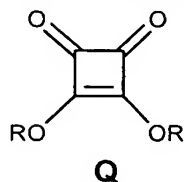
a hydrogenation catalyst selected from the group consisting of: Pd/C, Pt/C, PdOH, and Raney nickel; and

a solvent selected from the group consisting of: THF, methanol, ethanol, propanol, isopropanol, acetonitrile, ethyl acetate, and mixtures thereof; and

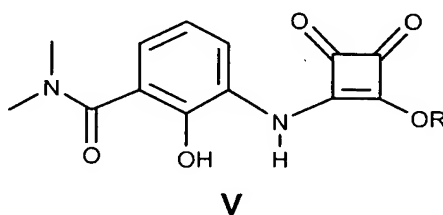
pressurizing the resulting mixture under hydrogen at a pressure of about 10 to about 500 psi to produce the intermediate compound of formula **IV(i)**:



(c) adding the compound of formula **Q**:

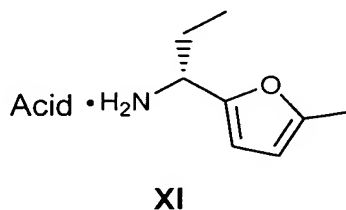


in a concentration of at least 1 molar equivalent with respect to the compound of formula **IV(i)**, to the reaction mixture comprising the compound of formula **IV(i)** obtained in step (b), and adjusting the temperature to about 0 °C to about 80 °C to produce a compound of formula **V**:



wherein R in said compound of formula **Q** is selected from the group consisting of: methyl, ethyl, propyl and isopropyl, and wherein said reaction is optionally catalyzed by a base selected from the group consisting of: KOH, NaOH, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, KHCO<sub>3</sub>, tetramethylguanidine, DBU, diisopropylethylamine, and mixtures thereof;

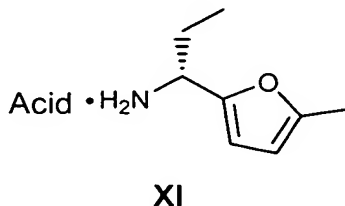
(d1) mixing: the compound of formula **V** from step (c) with the compound of formula **XI**



and a base in a solvent, heating the resulting reaction mixture to a temperature of about 20 °C to about 150 °C, and then acidifying the reaction mixture to a pH of about 3 to about 7, to produce a compound of formula **I**; said base being selected from the group consisting of: pyridine, dimethylaminopyridine (DMAP), diisopropylethylamine and -N(R<sup>2</sup>)<sub>3</sub>; wherein each R<sup>2</sup> is independently selected from the group consisting of:

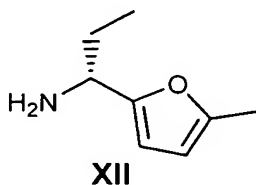
alkyl and cycloalkyl; and said base being used in a concentration of at least about 1 molar equivalent with respect to the compound of formula **IV**; and said solvent being selected from the group consisting of: nitrile, ether, and alcohol solvents; or

5 (d2) mixing the compound of formula **XI**:



with water and solvent selected from the group consisting of: ethers and methylene chloride;

10 basifying the resulting reaction mixture in a base selected from the group consisting of: NaOH, KOH, Mg(OH)<sub>2</sub>, Na<sub>2</sub>CO<sub>3</sub> and K<sub>2</sub>CO<sub>3</sub>, to a pH of about 7 to about 14, said basification being done at a temperature of about 0°C to about 50 °C to produce a compound of formula **XII**:

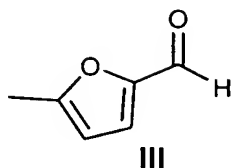


15 dissolving said compound of formula **V** from step (c) in a solvent selected from the group consisting of: alcohol solvents, nitrile solvents, ether solvents and toluene;

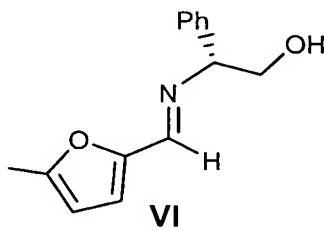
mixing the resulting solution with the compound of formula **XII**, and optionally adding a catalytic amount of a base to the resulting solution, wherein said base is  
20 selected from the group consisting of: pyridine and -N(R<sup>3</sup>)<sub>3</sub>, wherein R<sup>3</sup> is selected from the group consisting of: alkyl, aryl, aralkyl, and arylalkyl, and wherein the temperature of the resulting solution is about 10 °C to about 150 °C, to produce a compound of formula **I**;

25 (e) wherein said compound of formula **XI** is prepared by:

mixing the compound of formula III:

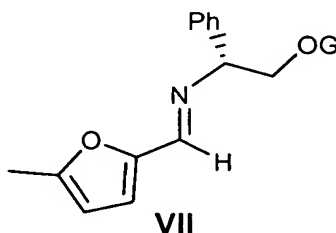


5 with 0.01 molar equivalent, with respect to the compound of formula III, of R-2-(-)-phenylglycinol in a solvent selected from the group consisting of: aromatic solvents, halogenated solvents, alcohol solvents, nitrile solvents, ether solvents, and mixtures thereof, and heating the resulting mixture at reflux to produce a compound of formula VI:



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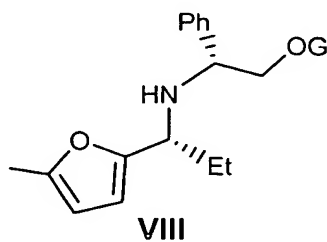
mixing the solution comprising the compound of formula VI with a silylating reagent selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein the TMS chloride or TMSOTF is used in combination with an aryl or alkyl base, and an acid in a concentration of at least about 0.2 molar equivalent  
15 with respect to the compound of formula VI, said acid being selected from the group consisting of: ammonium sulphate, ammonium nitrate, ammonium chloride, H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, citric acid, mesyl chloride, paratoluenesulfonic acid, paratoluenesulfonic acid pyridinium salt, and alkylsulfonic acid, and heating the resulting reaction mixture  
20 at reflux to produce an imine compound of formula VII:



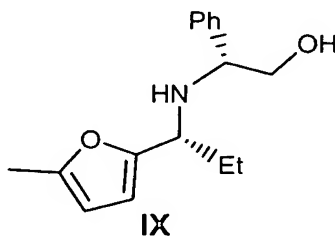
wherein G represents a protecting group that is the silylating reagent used;



mixing said imine compound of formula **VII** with an organometallic reagent in a solvent at a temperature of about 0 °C to about 80 °C, said organometallic reagent being selected from the group consisting of: diethyl zinc, ethylzinc bromide, ethylzinc chloride, ethylmagnesium bromide, ethylmagnesium chloride and ethyllithium, said organometallic reagent being used in a concentration of 0.1 to about 5 molar equivalents with respect to the compound of formula **VII**, said solvent being selected from the group consisting of: benzene, toluene, TBME, THF, DME, dimethoxyethane, and mixtures thereof, to produce a compound of formula **VIII**:



adding the compound of formula **VIII** to a cooled aqueous acid, said acid being at a concentration of about 2.5 to about 5 molar equivalents with respect to the compound of formula **VIII**, adding water and a cosolvent and mixing the resulting mixture, adding a base to said mixture to adjust the pH of the aqueous phase to about 9 to about 13, to produce a compound of formula **IX**:



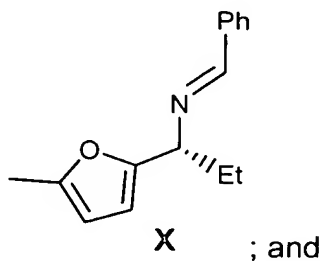
said co-solvent being selected from the group consisting of: methanol, ethanol, propanol, isopropanol, butanol, sec-butanol, pentanol, hexanol, heptanol, octanol, and mixtures thereof,

said base being selected from the group consisting of: ammonium hydroxide, metal hydroxide, metal oxide, metal carbonate, metal bicarbonate, and mixtures thereof, wherein said metal is selected from the group consisting of: lithium, sodium, potassium, rubidium, cesium, beryllium, magnesium, calcium, strontium, barium, aluminum, indium, thallium, titanium, zirconium, cobalt, copper, silver, zinc cadmium, mercury and cerium, or

said base being selected from the group consisting of: a metal salt of a (C<sub>1</sub>-C<sub>12</sub>)alkanol and a (C<sub>3</sub>-C<sub>12</sub>)cycloalkanol, wherein the metal is selected from the group consisting of: Li, Na, K, and Mg;

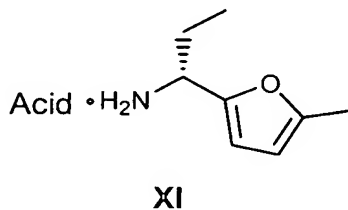
dissolving the compound of formula IX in solvent selected from the group consisting of: water, methanol, ethanol, propanol, isopropanol, butanol, sec-butanol, pentanol, hexanol, tetrahydrofuran, 1,2-dimethoxyethane, 1,2-diethoxymethane, diglyme, 1,4-dioxane, and mixtures thereof,

cooling the resulting solution to a temperature of about -5 °C to about 20 °C, adding R<sup>4</sup>NH<sub>2</sub> to said solution, and then adding an agent selected from the group consisting of: NaIO<sub>4</sub>, Pb(OAc)<sub>4</sub>, H<sub>5</sub>IO<sub>6</sub>, and mixtures thereof, to produce a compound of X:



wherein R<sup>4</sup> is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and aralkyl;

dissolving the compound of formula X in a solvent and adding the resulting solution to an acid solution at a temperature ranging preferably from about -50 °C to about 80 °C to produce the compound of formula XI:



said compound XI being a salt,

wherein said solvent is selected from the group consisting of: hydrocarbon solvents and ethers and mixtures thereof, and

said acid is selected from the group consisting of: sulfonic acids, tartaric acids, H<sub>2</sub>SO<sub>4</sub>, HCl, H<sub>3</sub>PO<sub>4</sub>, HBr, carboxylic acids and mixtures thereof.

75. The process of Claim 74 wherein:

in step (a), the preparation of the compound of formula **IV**, the reaction  
the reaction mixture of said compound of formula **II** and said acid chloride is 40°C to  
about 90°C, said dimethylamine is at a concentration of at least about 2 molar  
5 equivalents with respect to the compound of formula **II**, said temperature of said  
reaction mixture is about 0°C to about 25°C, said reaction mixture is acidified to a pH  
of about 1 to about 5, said acid for said aqueous acid is selected from the group  
consisting of: HCl, H<sub>2</sub>SO<sub>4</sub>, H<sub>3</sub>PO<sub>4</sub>, and mixtures thereof;

in step (b), the hydrogenation of the compound of formula **IV**, said base  
10 is selected from the group consisting of: Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, and mixtures thereof, said  
base is used at a concentration of about 1.05 to about 1.5 molar equivalents, said  
catalyst is selected from the group consisting of Pd/C and PdOH, said solvent is  
selected from the group consisting of: methanol, ethanol, propanol, isopropanol, and  
mixtures thereof, and said hydrogen pressure is about 20 to about 200 psi psi;

15 in step (c), the reaction of the compound of formula **Q** with the  
compound of formula **IV(i)**, the compound of formula **Q** is used at a concentration of  
about about 1 to about 2 molar equivalents, said temperature is about 20 °C to about  
50 °C, and said optional base is selected from the group consisting of: Na<sub>2</sub>CO<sub>3</sub>,  
K<sub>2</sub>CO<sub>3</sub> and mixtures thereof;

20 in step (d1), the reaction of the compound of formula **V** with the  
compound of formula **XI**, said base is used in an amount of about 1 to about 2 molar  
equivalents with respect to the compound of formula **V**, said solvent is selected from  
the group consisting of alcohol and nitrile solvents, said temperature is about 40 °C to  
about 80 °C, and said pH is about 3 to about 5;

25 in step (d2), the reaction of the compound of formula **V** with the  
compound of formula **XII**:

said mixture with said compound of formula **XI** is basified with  
NaOH or KOH to a pH of about 10 to about 14 at a temperature of about 10 °C to  
about 40 °C to produce said compound of formula **XII**,

30 said compound of formula **V** is dissolved in an alcohol solvent,  
said compound of formula **XII** being used at a concentration about  
1 molar equivalent with respect to the compound of formula **V**,

said catalytic base being selected from the group consisting of: pyridine and  $-N(R^3)_3$  wherein each  $R^3$  is independently selected from the group consisting of ethyl, isopropyl, propyl, butyl, phenyl, tolyl and benzyl, and

said temperature of said resulting solution with the compound of formula **XII** being about 40 °C to about 80 °C;

in step (e), in the reaction to produce the compound of formula **VI** from the compound of formula **III**, said R-2-(-)-phenylglycinol is in a concentration of about 0.5 to about 1.5 molar equivalents, and said solvent for said R-2-(-)-phenylglycinol is selected from the group consisting of: benzene, toluene, dichloromethane, methylene chloride, chlorobenzene, methanol, ethanol, propanol, isopropanol, n-propanol, butanol, acetonitrile, THF and t-butylmethylether;

in step (e) in the reaction to produce the compound of formula **VII** from the compound of formula **VI**, said silylating reagent is selected from the group consisting of: hexamethyldisilazane, TMS chloride, and TMSOTF, wherein the TMS chloride or TMSOTF is used in combination with triethylamine, and said acid is selected from the group consisting of: ammonium sulphate, ammonium nitrate and ammonium chloride, said acid at a concentration of at least about 0.4 molar equivalents with respect to the compound of formula **VI**;

in step (e), in the reaction to produce the compound of formula **VIII** from the compound of formula **VII**, said organometallic reagent is used in a concentration of about 1 to about 5 molar equivalents with respect to the compound of formula **VII**, said solvent is selected from the group consisting of: THF, TBME, and mixtures thereof, and said temperature is about 10 °C to about 50 °C;

in step (e), in the reaction to produce the compound of formula **IX** from the compound of formula **VIII**, said cooled aqueous acid is at a temperature of about 0 °C to about 15 °C, said acid is selected from the group consisting of:  $H_2SO_4$ , HCl,  $H_3PO_4$ , and mixtures thereof, said acid is in a concentration of about 2.5 to about 3 molar equivalents with respect to the compound of formula **VIII**, said cosolvent is selected from the group consisting of: methanol, ethanol, propanol, isopropanol, butanol, sec-butanol, pentanol, hexanol, heptanol, octanol, and mixtures thereof, said base is selected from the group consisting of: KOH, NaOH,  $NH_4OH$ , LiOH and CsOH, and said pH is adjusted to about 10 to about 11,

in step (e), in the reaction to produce the compound of formula **X** from the compound of formula **IX**, the resulting solution is cooled to about 0 °C to about 15 °C, and said  $R^4$  is a (C<sub>1</sub>-C<sub>3</sub>)alkyl; and

5 in step (e), in the reaction to produce the compound of formula **XI** from the compound of formula **X**, said compound of formula **XI** is dissolved in a solvent selected from the group consisting of: toluene, xylene, chlorobenzene, dichlorobenzene, diethyl ether, dipropyl ether and dibutyl ether, 1,2-dimethoxyethane, 1,2-diethoxyethane, diglyme, 1,4-dioxane, tetrahydrofuran and mixtures thereof, said acid in said acid solution is selected from the group consisting of: paratoluene sulfonic  
10 acid and alkylsulfonic acids, and said temperature is about -20 °C to about 20 °C.

76. The process of Claim 75 wherein:

in step (a), the preparation of the compound of formula **IV**, said compound of formula **II** is dissolved in acetonitrile and thionyl chloride, said  
15 temperature is about 65°C to about 75°C, said dimethylamine is dissolved in acetonitrile, said dimethylamine being at a concentration of about 2.5 molar equivalents with respect to the compound of formula **II**, said temperature of said reaction mixture is about 5°C to about 10°C, said reaction mixture is acidified to a pH of about 2 to about 3, said aqueous acid is H<sub>2</sub>SO<sub>4</sub>, and said substituent A is Br;

20 in step (b), the hydrogenation of the compound of formula **IV**, said base is K<sub>2</sub>CO<sub>3</sub> used at a concentration of about 1.05 to about 1.1 molar equivalents, said catalyst is Pd/C, said solvent is ethanol, and said hydrogen pressure is about 100 to about 120 psi;

in step (c), the reaction of the compound of formula **Q** with the  
25 compound of formula **IV(i)**, the compound of formula **Q** is used at a concentration of about 1.3 to about 1.5 molar equivalents, said temperature is about 25 °C to about 35 °C, R is ethyl, and said optional base is K<sub>2</sub>CO<sub>3</sub>;

in step (d1), the reaction of the compound of formula **V** with the compound of formula **XI**, the compound of formula **XI** is used in an amount of about 1.1 molar equivalents, said base is triethylamine used in an amount of about 1.3 to about 1.5 molar equivalents with respect to the compound of formula **V**, said solvent is acetonitrile, said temperature is about 60 °C to about 70 °C, and said pH is about 4;

in step (d2), the reaction of the compound of formula **V** with the compound of formula **XII**, said solvent used with said compound of formula **XI** is t-butyl methyl ether, said mixture with said compound of formula **XI** is basified with NaOH to a pH of about 12.5 to about 13.5 at a temperature of about 20 °C to about 30 °C to produce said compound of formula **XII**, said compound of formula **V** is dissolved in the solvent n-propanol, said compound of formula **XII** being used at a concentration about 1.1 molar equivalents with respect to the compound of formula **V**, said catalytic base being diisopropylethylamine, said temperature of said resulting solution with the compound of formula **XII** being about 60 °C to about 70 °C

in step (e), in the reaction to produce the compound of formula **VI** from the compound of formula **III**, said R-2-(-)-phenylglycinol is in a concentration of about 0.9 to about 1.1 molar equivalents, and said solvent for said R-2-(-)-phenylglycinol is THF;

in step (e) in the reaction to produce the compound of formula **VII** from the compound of formula **VI**, said silylating reagent is hexamethyldisilazane, and said acid is ammonium sulphate at a concentration of at least about 0.5 molar equivalents with respect to the compound of formula **VI**;

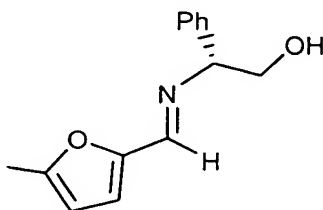
in step (e), in the reaction to produce the compound of formula **VIII** from the compound of formula **VII**, said organometallic reagent is ethylmagnesium bromide used in a concentration of about 2 to about 3 molar equivalents with respect to the compound of formula **VII**, said solvent is TBME, and said temperature is about 20 °C to about 35 °C;

in step (e), in the reaction to produce the compound of formula **IX** from the compound of formula **VIII**, said cooled aqueous acid is at a temperature of about 0 °C to about 10 °C, said acid is H<sub>2</sub>SO<sub>4</sub>, said acid is in a concentration of about about 2.5 molar equivalents with respect to the compound of formula **VIII**, said cosolvent is sec-butanol, said base is NH<sub>4</sub>OH, and said pH is adjusted to about 11,

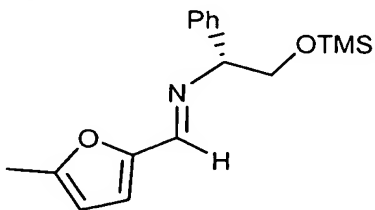
in step (e), in the reaction to produce the compound of formula **X** from the compound of formula **IX**, said compound of formula **IX** is dissolved in ethanol and the resulting solution is cooled to about 0 °C to about 10 °C, said R<sup>4</sup> is methyl, and said agent is NaIO<sub>4</sub>; and

in step (e), in the reaction to produce the compound of formula **XI** from the compound of formula **X**, said compound of formula **XI** is dissolved in THF, said acid in said acid solution is paratoluene sulfonic acid, and said temperature is about 0 °C to about 10 °C.

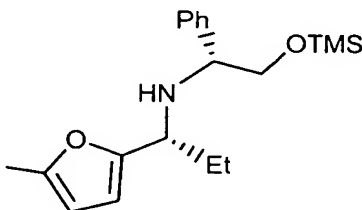
77. A compound of the formula:



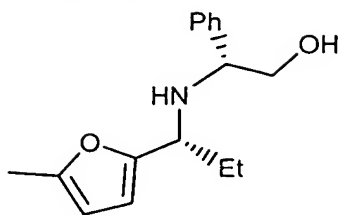
78. A compound of the formula:



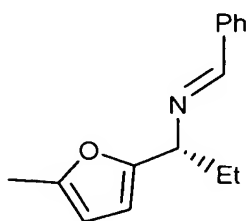
79. A compound of the formula:



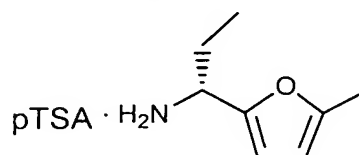
80. A compound of the formula:



81. A compound of the formula:



82. A compound of the formula:



83. A compound of the formula:

